Production of antimicrobial plastic articles, especially catheters, involves pretreatment with colloidal metal, especially colloidal silver, before the final moulding process

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Abstract of DE 19936059 (A1)

A process for the production of antimicrobial plastic products by shaping a pre-product, in which at least one component of the pre-product is treated with a metal colloid before the forming procedure. An independent claim is also included for plastic products obtained by this process.

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1. Method to the production of an antimicrobial plastic body, of a comprising moulds precursor, characterised in that before that moulds at least an ingredient of the precursor with a metal colloid treated becomes.

2. Process according to claim 1, whereby the precursor consists several polymeric materials of or.

3. Process according to claim 2, whereby the precursor consists of polyurethane.

4. Process according to one of claims 1 to 3, whereby the plastic before product beside the polymeric materials other additives become added.

5. Process according to claim 4, whereby the additives consist of inorganic particles.

6. Process according to claim 5, whereby the inorganic particles cover barium sulfate, calcium sulfate, Strontiumsulfat, titanium oxide, alumina, silicon oxide, zeolites, mica, talc or kaolin.

7. Process according to claim 6, whereby the inorganic particles cover barium sulfate.

8. Process according to one of claims 1 to 7, whereby or the several Vorprodukteteilstandteile with colloids the metal treated become.

9. Process according to one of claims 4 to 7, whereby both the plastic and the inorganic particles with colloids the metal become treated.

10. Process according to one of claims 4 to 7, whereby the inorganic particles with the metal colloid become treated.

11. Process according to one of claims 1 to 10, whereby the metal colloid is colloidal silver.

12. Process according to one of claims 1 to 11, whereby the treated precursor by mixing, a kneading, extrusion, injection moulding or (hot ones) press into the final form brought becomes.

13. Plastic body available after one of the claims 1 to 12.

14. Plastic body according to claim 13 in mould of a catheter.

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The invention relates to methods to the production of antimicrobial metalliferous plastic bodies, in particular subject-matters for the medical need. These subject-matters become in particular used in the form of catheters.

A significant disadvantage of plastic articles for the medical need, in particular of short and long-term catheters insists those in the light settling barness of the used plastics with often multi-resistant germs, on the surface of the plastic body, and/or. on the catheter outside and - inside, a biofilm form. A prophylactic impregnation of the surfaces with antibiotics separates because of the high selection of resistant micro organisms, connected thereby.

In the last years therefore numerous experiments were undertaken, the plastic surfaces with silver ions, the z. B. from silver nitrate, - acetate, - chloride originate to impregnate. Silver ions possess a very wide antimicrobial spectrum and an high toxicity from all heavy metal ions opposite micro organisms by z. B. the connection to the cell wall over SH group, blockage of the breathing chain, preventing the cell proliferation by DNA connection, but a low toxicity opposite animalischen cells. Here however no sufficient microbial effectiveness could become observed in various clinical studies. Additional one leads the corrosive action and/or. the poor water solubility from silver salts to other problems in the application.

With contact of metal surfaces such as z. B. Silver with physiological NaCl solution becomes in depending on the size of the metal surface metal ions (silver ions) in freedom set. The admixture of metal powder, z. B. of silver powder, to a polymer, z. B. Polyurethane, does not lead however to the success, since are required due to the small surface relative high concentrations at metal powders, which mechanical problems in the plastic material caused. The critical surface required for an antimicrobial effectiveness is not more attainable therefore by adding metal powder.

EP-A-0 711,113 a disclosed new technology, with the metallic silver on PU foils evaporated and these in comminuted mould to be compoundiert. Thus an even distribution of silver particles in the polymer material could become achieved and thus a large surface area achieved sufficient for a bakteriostatischen effectiveness. The antimicrobial effectiveness of these plastic bodies is both very good occupied regarding reduction and prevention of adherence, bio film formation and long-term behaviour and toxicity and compatibility. The applicability of foregoing plastic bodies becomes however above all caused by a time-consuming and cost-intensive manufacturing process, by vaporizing with silver, limited.

The object of the instant invention is thus the provision of a method to the production of antimicrobial effective plastic bodies, which do not exhibit the foregoing disadvantages, D. h. simple are producible and a sufficient silver ion concentration at the surface supply.

Dissolved one becomes this object by a method, which is characterized by the fact that before that moulds of the plastic body at least an ingredient of the precursor of the moulding with a silver colloid treated becomes.

As starting material for the plastic body many polymeric compounds come into considerations, which become usually used in the medical range. These are in particular polyethylene, polypropylene, crosslinked polysiloxanes, polyurethanes, polymers on (Meth) acrylate basis, cellulose and cellulose derivatives, polycarbonates, ABS, Tetrafluorethylenpolymere and polyethylene terephthalates, as well as corresponding copolymers. Particularly prefered is polyurethane, polyethylene and polypropylene as well as polyethylene polypropylene copolymers. The inserted metal is preferably silver, copper, gold, zinc or cerium. From these metals silver is particularly prefered.

Beside the colloidal metal or several polymeric materials an inserted becomes with the production of the plastic bodies according to invention. The mixture from kolloidem metal and plastic (EN) also other additives can become added. These are in particular inorganic particles such as barium sulfate, calcium sulfate, Strontiumsulfat, titanium oxide, alumina, silicon oxide, zeolites, mica, talc, kaolin etc. Particularly prefered is thereby barium sulfate, which can serve simultaneous as Roentgen contrast means for special embodiments.

Before that moulds or several polymer components with the colloidal metal solution a treated becomes and/or or the several inorganic additives.

After mixing (partly) the starting materials treated with a colloidal metal the obtained mixture becomes processed, around plastic fresh product obtained. This can in mixers, kneaders, extruders, injection moulding machines or (hot ones) presses to happen.

The metal colloids with those the plastics or inorganic particle treated become, place one suitable-prove by reduction from metallic salt solutions. The stabilization of the resultant colloid protective agents can become such as gelatin, silicic acid or starch inserted.

In case of the preferred metal silver becomes z. B. ammoniakalische silver nitrate solution in the gelatin slow with a suitable reducing agent staggered. As reducing agents can beside aldehydes (z. B. Acetaldehyde) also Aldosen (z. B. Glucose), quinones (z. B. Hydroquinones), inorganic complex hydrides (sodium or Calliumboranat), reducing nitrogen compounds (hydrazine, polyethyleneimine) as well as ascorbic acid used become plastic before products, like z. B. Pellet, and/or the inorganic particles, like z. B. Barium sulfate, then treated, dried and into the corresponding mould brought becomes with this colloidal silver solution. Applying of the silver colloid on the starting materials and subsequent drying can become several times repeated, so that very high silver concentrations into the plastic material introduced to become in this way to be able. This is in particular favourable during the silver coating of barium sulfate, since so a previous coating of the plastic pellets is not compellingly required.

The use of z. B. Can be omitted to gelatin or starch as colloid stabilizer with the adsorption of silver the inorganic particles, since the microcrystalline silver particle resultant with the reduction to the surface of the inorganic particles bonded become adsorbtiv and thus the formation of a closed silver layer on the solid prevented becomes.

By variation or omitting the colloid stabilizers as well as the reducing agents the particle size of the silver and thus the mobility of the resultant silver ions in a wide range can beyond that become controlled and by the use of low molecular aldehydes as reducing agents, which partly interlace the gelatin, one much good adhesion on the polymer achieved.

In the following the invention process becomes illustrated by examples.

Example 1

Production of the silver colloid

1.0 g gelatin (DAB) are dest with 40 DEG C in 100 ml aqua. bottom agitations dissolved. For this one gives AgNO3 p to subsequent 1.0 g (5.88 mmol). A. and the staggered developed solution with 1,0 ml (14.71 mmol) 25%-igen NH3-Wasser.

To the illustration of the silver colloid to foregoing solution with 40 DEG C slow over a period of 30 min 258.7 mg (5.88 mmol, 330 mu l) are dest acetaldehyde dissolved in 50 ml aqua. dropped.

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Example 2

Coating of PU pellets

10 min after terminated Zutropfen in accordance with example 1 becomes approx. 50 g PU pellets from Tecothane TT-1085A added and for coating with colloidal silver first 2 h with 40 DEG C and subsequent 3 h with blank vigorous agitated.

One separates the silver colloid off by rapid filtration over a Faltenfilter suitable pore size, washes the pellets again with the filtrate after and the transfered still moist pellets into an evaporating dish. After the removal excess silver colloid solution adherent at the polymer 10 h do not become dried with 70 DEG C.

Example 3

Adsorption of kolloidalem silver at barium sulfate

One adds 50 g BaSO4 to the aqueous ammoniakalischen solution from silver nitrate and gelatin, described in the example, and staggered this suspension analogous example 1 slow with an aqueous solution of the reducing agent with 40 DEG C. Thus the formed silver colloid direct adsorbs itself to the BaSO4 acting as Roentgen contrast means. The suspension will subsequent by evaporation with 75 DEG C of the water freed and can as anhydrous solid in homogeneous and good compoundierbarer mould obtained become.

Example 4

Alternative adsorption of colloidal silver at barium sulfate

In accordance with example 3 resulting suspension from silver nitrate, gelatin and barium sulfate becomes by filtration of the solvent and subsequent by washing afterwards first with approx. 5% ammonia solution and then several times with aqua dest. of all low molecular organic compounds freed. The filter arrears supply analogous example 3 an homogeneous material after air-drying with 75 DEG C. Also this process can become several times repeated.

Example 5

Determination of the antibacterial effectiveness

To the determination of the settling barness of the plastic bodies according to invention with germs in each case five cylindrical samples of the corresponding plastic (diameter 3 mm, length 13 mm) with a composition contained staphylococcus epidermis in a Trypcase Soy Broth nutrient solution were inkubiert with 175 DEG C. The subsequent plastic bodies became examined (number 1 are commercial and untreated, number 2 and 3 are according to invention):
Specimen 1: Piece from a PU-catheter of the company Arrow (it 04701)
Specimen 2: in accordance with example 2 of the instant invention
Specimen 3: in accordance with example 3 of the instant invention.

Those in each case 5 specimens were submitted four test rows the bottom subsequent conditions:
Test row 1: initial concentration of staphylococcus epidermis 5 x 10< 7> CFU/ml
Test row 2: initial concentration of staphylococcus epidermis 10< 8> CFU/ml
Test row 3: like test row 1, however still another 5-stündigen Vorinkubation in physiological buffer solution with 37 DEG C measured
Test row 4: like test row 1, whereby the plastic bodies with sterile filtered natural urine became with 37 DEG C 4 hours prolonged pretreated.

Table 1 shows the number of the settled plastic bodies. Certain one became this by visual control.

Table 1
EM16.1

The catheter materials do not show impairment of the mechanical properties necessary for therapeutic purposes (roughness, homogeneity and resilience) after the Compoundieren. Here the method can become good at alternate requirements in the production process adapted, there the antimicrobial effectiveness independent of it obtained remains whether the silver over a coating of the PU pellets (example 2) or over the Roentgen contrast means (example 3 and 4) into the polymer material introduced becomes.

The plastic articles according to invention show a significant higher antimicrobial effectiveness regarding adherence and bio film formation as well as a remarkably improved long-term behaviour than prior materials with comparable low toxicity.

The production processes according to invention are good controllable, inexpensive and suitable for a production in the larger yardstick. To remove additional one prepared with example 4 a method all "auxiliary chemicals" from the inorganic contrast agent, so that a certifying of the method should not prepare problems.

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